

Neonatal COVID-19 Infection - A Case Series from a Tertiary Care Government-Designated COVID-19 Hospital in India

Running title: COVID-19 Disease in Preterm Neonates: Management and Outcome

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Abstract: COVID-19 disease was pronounced a pandemic by World Health Organization (WHO) on 11th March 2020. Although children seem to have less severe clinical symptoms when infected, the potential harm of this novel disease remains largely unknown in neonates, especially in preterm infants. There is little literature available about the clinical features, outcomes, and the mode of transmission of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in neonates, especially from India. The paucity of data on neonates, especially in preterm and low birth weight babies, makes diagnosis and management of such babies a challenging task. We present a case series of neonates with SARS-CoV-2 disease with details of their clinico-radiological profiles and management from our tertiary-care government-designated COVID-19 hospital admitted in the period from January 2021 to March 2022. These neonates presented with mild to moderate respiratory distress with hypoxia. HRCT chest was done for all the cases which showed variable degrees of pulmonary involvement. They responded well to humidified Oxygen therapy.

Keywords: COVID-19, Neonate, Management, Outcome

1. Introduction

In contrast to older children and adults, COVID-19 in neonates remains uncommon. While the disease has a widespread clinical profile and its impact has been well-recognized in certain age groups, the effects, both direct and indirect, on the neonatal population remain largely unknown. On review of analysis from a large neonatal coronavirus disease 2019 (COVID-19) registry under the National Neonatology Forum (NNF) of India, a total of 1713 neonatal cases were reported between April 2020 to March 2021 out of which 20.7% neonates were premature. (1)

The clinical picture of Coronavirus 2 (SARS-CoV-2) positive neonates is highly variable. (2) SARS-CoV-2 infection can range from asymptomatic infection, rhinorrhoea, feeding difficulty, and hypoxia to severe respiratory distress in neonates. (2)

Our institute being a tertiary care Designated COVID 19 government hospital in a major metropolitan city of India, we had 472 deliveries of COVID-19 affected mothers between January 2021 - March 2022. We had 19 COVID-19 neonatal cases during this period.

We report 4 cases of neonatal COVID-19 disease in preterm-low birth weight babies with their clinical profiles.

Clinical Description:

Case 1

A 13 days old male baby brought with complaints of cough and cold for 1 day. There was no fever. The baby was born at a private health care facility at 31 weeks of gestation with a birth weight of 1.7 kg delivered by a vaginal delivery. The baby was kept in NICU for preterm low birth weight care at referring private hospital.

On Day 13, he had developed cough with increased respiratory activity, hence tested for COVID-19 Rapid Antigen Test and referred to us after testing positive. On admission, he was eutermic, heart rate-138/minute, respiratory rate-66/minute, mild subcostal retractions were present with SPO₂ of 86% on room air. Chest was clear on auscultation. The baby was kept on O₂ with FiO₂ at 30-35%. Orogastric tube feeds were continued. Sepsis screen was negative. 2D echocardiography was normal.

Chest X ray was suggestive of right sided homogenous opacities, suspecting COVID 19 pneumonia, repeat confirmatory test (Rapid antigen) done at our hospital for

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SARS COV-19 was also positive. The mother's nasopharyngeal swab for COVID-19 RTPCR was tested negative. CT scan of chest was performed to evaluate the extent of the disease which revealed confluent areas of consolidation in dependent upper and lower lobes of bilateral lungs. Discrete areas of ground glass opacities noted adjacent to the areas of consolidation reported as likely of COVID pneumonia (CORAD 6, CT Severity score 5/25). (Figure 1)

The baby was put on humidified O₂ with blender FiO₂ of 30-35%. The baby responded well to O₂ therapy.

Baby was gradually weaned off O₂ over 1 week and discharged with good weight gain.

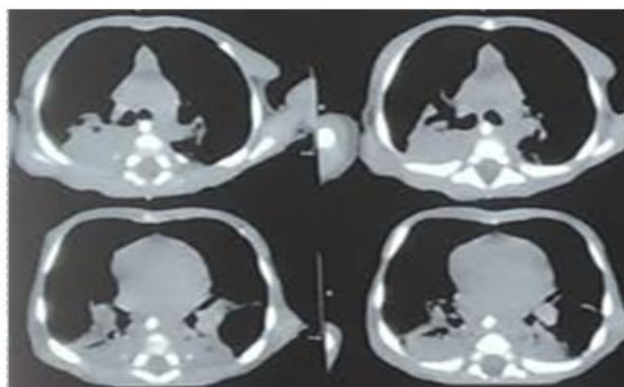


Figure 1: HRCT Chest of case 1-showing confluent areas of consolidation in dependent upper and lower lobes of bilateral lungs with discrete areas of Ground-Glass Opacities noted adjacent to the areas of consolidation

Case 2

A 5-day-old male baby was referred to us with SARS COVID-19 RTPCR positive status. The baby was born at 30 weeks of gestation with a birth weight of 1.43 kg. The baby was kept on bubble CPAP and received surfactant at 2 hours of life. The baby was weaned off O₂ by day 3 of life.

At admission, the baby was maintaining saturation on room air and was tolerating Oro-Gastric tube feeds. He started gaining weight adequately. On the 18th day of life, the baby developed respiratory distress in the form of tachypnea with a respiratory rate of 78/minute without subcostal and lower intercostal retractions but associated with a drop in saturation of 78-80%.

The child was kept under O₂ with FiO₂ of 35% and was closely monitored. The septic screen was negative.

CT scan was done in view of suspicion of COVID 19 pneumonia. It revealed subtle areas of Ground Glass Opacities (GGOs) in the dependent portion of bilateral lower lobes (right>left), predominantly peripheral in location. Findings were suggestive of typical COVID pneumonia with CORADS-6 and CT severity score - of 5/25. (Figure 2)

The baby was managed conservatively with O₂ therapy alone. During the course of the illness, the baby was gaining weight adequately. The baby responded to O₂ therapy well and was gradually weaned off O₂. The baby was discharged on DOL 28 with a weight of 1.89 kg.

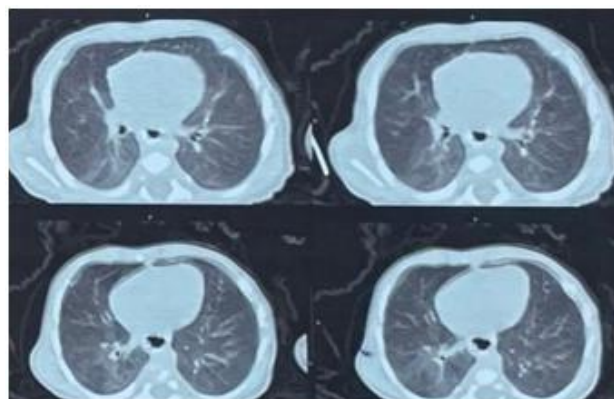


Figure 2: HRCT Chest of case 2-showing subtle areas of Ground Glass Opacities (GGOs) in the dependent portion of bilateral lower lobes (right>left)

Case 3

An inborn baby was born at 27 weeks of gestation with a birth weight of 1.1 kg. She was admitted to NICU and received surfactant on DOL1 for hyaline membrane disease. Baby was weaned off O₂ By DOL 7 and afterward kept for weight gain.

On day 28, baby developed desaturations reaching up to 85% from previous SPO₂ of 94-97% and had tachypnea of 70 / minute. On auscultation the chest was clear. Baby was investigated for these complaints. The septic screen was negative. 2D Echocardiography was normal. Chest X-ray was grossly normal.

Baby was kept under O₂ with fiO₂ 35-45%. Over the next three days, the baby started developing further desaturations up to 60-70% even if O₂ was interrupted for a few seconds and getting corrected immediately with O₂ therapy, without any signs of increased work of breathing in the form of intercostals / subcostal retractions or grunting. During this period, she was tolerating orogastric tube feeds well and weight gain continued. Hence COVID-19 was suspected and investigations were sent. RTPCR for COVID-19 was reported negative. However, COVID IgG antibodies of mother and baby were positive. X-ray chest was reported as normal. Hence, the HRCT chest was done. It was reported as CORADS 6 and CT severity score of 4/25 with findings of few discrete areas of rounded, almost symmetrical Ground Glass Opacities (GGOs) in the bilateral lung parenchyma, in apical segments of upper lobe, and postero-basal segments of lower lobes, predominantly peripheral in distribution. (Figure 3)

The baby was managed conservatively with only O₂ supplementation. The baby gradually improved and was weaned off O₂ by DOL 50. Throughout this period, the baby was on full feeds and adequate and regular weight

gain was documented. The baby was discharged on DOL 58 with a weight of 1.89 kgs.

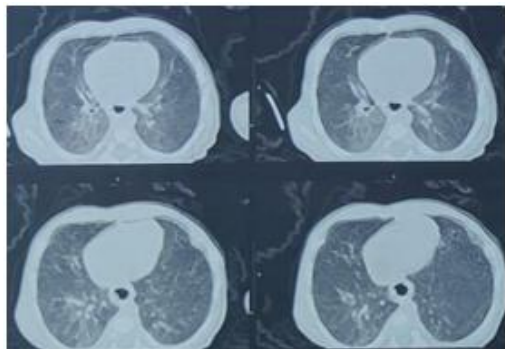


Figure 3: HRCT Chest-showing few discrete areas of Ground Glass Opacities (GGOs) in the bilateral lung parenchyma, in apical segments of upper lobe, and postero-basal segments of lower lobes, predominantly peripheral in distribution.

Case 4

A baby girl born at 30 weeks of gestation to a primiparous mother with a birth weight of 1 kg. Baby was weaned off CPAP by day 3 of life and was subsequently maintaining saturation on room air by DOL 8.

On day 14, desaturations up to 66-70% were noted, without any significant respiratory distress, and required O₂ therapy. The baby was investigated for this new onset hypoxia. 2D echo was normal. Septic screen and blood cultures were sterile. Chest X-ray was grossly normal. COVID RTPCR test was negative. SARS COV-2 IgG antibodies were tested positive. HRCT chest revealed ill-defined confluent areas of GGOs in the dependent segment of bilateral lower lungs. Patchy non-homogenous areas of consolidation with air bronchograms were seen in the right lung. Reported as finding suggestive of viral infective etiology? COVID-19 pneumonia.

The baby responded well to humidified O₂ therapy alone. Oxygen requirement decreased gradually over 3 weeks and the baby was maintaining saturation on room air by the 35th day of life. During this period the baby was on full feed and gaining weight. She was in NICU for another 2 weeks for weight gain and Kangaroo Mother Care. Further course in NICU was uneventful and discharged on day 50 of life with a weight of 1.8 Kgs.

Management and Outcome: All four neonates were managed conservatively with O₂ support. Feeding orogastric or oral was continued throughout the course of recovery with the duration of treatment being 14-22 days. All four cases continued to show weight gain in their NICU stay. No mortality was reported.

2. Discussion

In this case series, we report 4 neonates with COVID-19 disease presenting as tachypnea with mild to no respiratory distress, having hypoxia. All our neonates responded well to only humidified O₂ therapy and were

managed conservatively. As reported previously in a large cohort study by Kalamdani et al, most of the neonatal COVID-19 infection had asymptomatic to mild affection (3).

Detection of SARS-CoV-2 RNA by RTPCR on body fluids is considered the gold standard for diagnosis of COVID-19 (4). In our study, case 1 had with Rapid antigen test (RAT) for SARS-CoV-2 positive, case 2 was diagnosed with positive RTPCR on nasopharyngeal swab. Cases 3 and 4 tested RTPCR negative; however, had positive serology (IgG antibody) and radiological changes on the HRCT chest.

Transmission of SARS-CoV-2 may occur via the trans-placental route, or through environmental exposure to aerosolized droplets of viral particles after birth (2). All 4 of our neonates were hospitalized at birth and developed symptoms after 48 hours of life. All mothers were tested for COVID-19 RTPCR at the time of their hospitalizations and none of the four mothers were positive. This might suggest horizontal transmission of infection during NICU stay.

Clinical features of infected newborns, especially preterm infants, might be non-specific with respiratory distress being the most common (5). In a large cohort study by Chris Gale et al, the most common signs at presentation were hyperthermia and poor feeding or vomiting followed by rhinorrhea, respiratory signs, and lethargy. In a systemic review of Coronavirus infection in neonates by Trevisanuto D, et al the majority of neonates showed mild symptomstypical of acute respiratory infections such as fever, hypoxia and cough. (6) In a case series by Randad et al, preterm VLBW neonates developed mild rhinorrhea, fever, cough and hypoxia. This finding is similar to our cases. All four of our neonates had mild respiratory distress with tachypnea along with hypoxia. None of our babies developed temperature instability. Sepsis and bacterial pneumonia were ruled out based on negative sepsis screen as well as blood culture reports. (7)

The most common radiological findings in neonatal COVID-19 are multifocal and peripherally located ground-glass appearance starting from the lower lobes, accompanied by thickening in the interlobular septa, prominent vascular structures. In severe cases, a striking paving appearance and fragmented consolidation (8).

We performed HRCT chest to confirm diagnosis and to evaluate extent of lung involvement in all our cases while they were symptomatic which revealed peripheral ground glass opacities. This finding is similar to a neonatal COVID-19 case reported by Abasse et al in which the newborn developed an acute respiratory distress by 14 days of life with bilateral ground glass opacities on a chest CT scan (9). In a case report of severe COVID-19 pneumonia is a term neonate by Cakir et al, Chest CT findings showed bilateral ground-glass opacities, consolidation with surrounding halo sign, fine mesh shadow and tiny nodules fibrosis lesions and linear atelectasis. (10).

Based on current knowledge, treatment for SARS-CoV-2-positive newborns should be prevalently symptomatic or supportive (11). Our neonates responded well to O2 therapy only. The duration on treatment being 12-22 days. All four neonates were accepted feeds well during their treatment period and were discharged home with good weight gain.

3. Conclusion

This report summarizes the characteristics of COVID-19 in neonatal cases, with a focus on pulmonary involvement with striking feature of hypoxia disproportionate to respiratory distress. COVID-19 in newborn generally shows good prognosis. Treatment is prevalently symptomatic or supportive.

Lessons learnt:

Hypoxia is a striking feature of neonatal COVID-19 with pulmonary involvement.

Management of neonatal COVID-19 is conservative.

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Tables:

Table 1: Clinical features of the cases

Clinical features	Case 1	Case 2	Case 3	Case 4
Gender	Male	Male	Female	Female
Gestational age at birth (weeks)	31	30	27	30
Birth weight (kg)	1.7	1.43	1.1	1
Weight for GA	AGA	AGA	SGA	SGA
Age of presentation	13	18	28	14
Respiratory Findings	Tachypnea, mild retractions Desaturation up to 86%	Tachypnea Desaturation Subcostal and lower intercostal retractions	Tachypnea Desaturation up to 85%	No distress
Chest auscultation findings	Clear	Clear	Clear	Clear
O2 Support	O2 at flow 5L/min with blender FiO2 30-35%	O2 6L/min with blender FiO2 at 35%	O2 at 5L/min with blender FiO2 35-45%	O2 at 5L/min with blender FiO 35-40%
Duration of treatment	20 days	12 days	22 days	20 days
Chest radiography	Right sided Mid and upper zone homogenous opacities	Right upper zone homogenous opacities	Normal	Normal
CORADs	6	6	6	6
CT severity score	5/25	5/25	4/25	5/25
COVID RAT	Positive	-	-	Negative
COVID RT PCR	-	Positive	Negative	Negative

COVID antibody titres	-	SARS COV-2 IgG-31.85 (Positive)	SARS COV-2 IgG-18.1 (Positive)	SARS COV-2 IgG-22.4 (Positive)
Mothers COVID status	Negative	Negative	IgG Positive	Negative
Outcome	Discharged home	Discharged home	Discharged home	Discharged home
Duration of hospital stay	37 days	23 days	58 days	50 days
Mortality	Nil	Nil	Nil	Nil

Table 2: Laboratory features of the cases

Investigation	Reference Range*	Case 1	Case 2	Case 3	Case 4
Hb	-	16.5	15.9	16.7	18.9
TLC	-	9860	8900	9770	6890
PLT	-	208000	189000	246000	207000
CRP (mg/L)	0-6	3	1	3	3
Blood culture	-	Negative	Negative	Negative	Negative
FERRITIN (ug/L)	24-336	835	560	525	635
LDH (IU/L)	105-333	577	457	566	258

Hb-Haemoglobin; TLC-Total Leukocyte Count; PLT-Platelet count; CRP-C Reactive; LDH-Lactate Dehydrogenase.

*Reference Range as per laboratory